1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Insulin Glargine Formulation

Manufacturer or supplier's details
Company: Merck & Co., Inc
Address: 2000 Galloping Hill Road
         Kenilworth - New Jersey - U.S.A. 07033

Telephone: 908-740-4000
Emergency telephone number: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

2. HAZARDS IDENTIFICATION

GHS Classification
Skin corrosion/irritation: Category 2
Serious eye damage/eye irritation: Category 1
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Blood, Nervous system)

GHS label elements
Hazard pictograms:

Signal word: Danger

Hazard statements:
H315 Causes skin irritation.
H318 Causes serious eye damage.
H373 May cause damage to organs (Blood, Nervous system) through prolonged or repeated exposure if swallowed.

Precautionary statements:

Prevention:
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P280 Wear protective gloves/ eye protection/ face protection.

Response:
P302 + P352 IF ON SKIN: Wash with plenty of water.
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with...
water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/doctor.
P314 Get medical advice/attention if you feel unwell.
P332 + P313 If skin irritation occurs: Get medical advice/attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:
P501 Dispose of contents/container to an approved waste disposal plant.

Other hazards which do not result in classification
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Insulin Glargine</td>
<td>160337-95-1</td>
<td>&gt;= 60 &lt;= 100</td>
</tr>
<tr>
<td></td>
<td>m-Cresol</td>
<td>108-39-4</td>
<td>&gt;= 3 &lt; 5</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

General advice : In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

If inhaled : If inhaled, remove to fresh air.
Get medical attention if symptoms occur.

In case of skin contact : In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact : In case of contact, immediately flush eyes with plenty of water for at least 15 minutes.
If easy to do, remove contact lens, if worn.
Get medical attention immediately.

If swallowed : If swallowed, DO NOT induce vomiting.
Get medical attention if symptoms occur.

Most important symptoms and effects, both acute and delayed : Causes skin irritation.
Causes serious eye damage.
May cause damage to organs through prolonged or repeated exposure if swallowed.

Protection of first-aiders : First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).
5. FIREFIGHTING MEASURES

Suitable extinguishing media : Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media : None known.

Specific hazards during firefighting : Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products : Carbon oxides

Specific extinguishing methods : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.

Special protective equipment for firefighters : In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures : Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions : Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up : Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

7. HANDLING AND STORAGE
Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: Use only with adequate ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. Wash skin thoroughly after handling. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage: Keep in properly labelled containers. Keep tightly closed. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin Glargine</td>
<td>160337-95-1</td>
<td>TWA</td>
<td>50 µg/m3</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>50 µg/m3</td>
<td>Internal</td>
</tr>
</tbody>
</table>
| m-Cresol                | 108-39-4 | NAB (Inhalable fraction and vapor) | 20 ppm  
|                         |         |                               | 22 mg/m3                                      | ID OEL    |

Further information: Not classified as carcinogenic to humans. Not enough data to classify these materials as carcinogenic to humans or animals. Skin

<table>
<thead>
<tr>
<th>TWA (Inhalable fraction and vapor)</th>
<th>20 mg/m3</th>
<th>ACGIH</th>
</tr>
</thead>
</table>

Engineering measures: Ensure adequate ventilation, especially in confined areas. Minimize workplace exposure concentrations. Apply measures to prevent dust explosions. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment).
Personal protective equipment

Respiratory protection: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Combined particulates and organic vapour type

Hand protection:

Material: Chemical-resistant gloves

Remarks: Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

Eye protection: Wear the following personal protective equipment:
- Chemical resistant goggles must be worn.
- If splashes are likely to occur, wear: Face-shield

Skin and body protection: Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential.
- Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

Hygiene measures: If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
- When using do not eat, drink or smoke.
- Wash contaminated clothing before re-use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: Crystalline powder

Colour: white

Odour: No data available

Odour Threshold: No data available

pH: No data available

Melting point/freezing point: No data available

Initial boiling point and boiling range: No data available

Flash point: No data available

Evaporation rate: No data available

Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.
10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

Conditions to avoid : Heat, flames and sparks.
                      Avoid dust formation.
Incompatible materials : Oxidizing agents
Hazardous decomposition products : No hazardous decomposition products are known.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure : Inhalation
                                            Skin contact
Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity: Acute toxicity estimate: > 2,000 mg/kg
Method: Calculation method

Acute dermal toxicity: Acute toxicity estimate: > 2,000 mg/kg
Method: Calculation method

Components:
Insulin Glargine:
Acute oral toxicity: Remarks: No data available
Acute inhalation toxicity: Remarks: No data available
Acute dermal toxicity: Remarks: No data available

m-Cresol:
Acute oral toxicity: LD50 (Rat): 121 mg/kg
Remarks: Based on data from similar materials

Acute inhalation toxicity: Assessment: Corrosive to the respiratory tract.

Acute dermal toxicity: LD50 (Rabbit): 301 mg/kg
Remarks: Based on data from similar materials

Skin corrosion/irritation
Causes skin irritation.

Components:
Insulin Glargine:
Remarks: No data available

m-Cresol:
Species: Rabbit
Result: Corrosive after 3 minutes to 1 hour of exposure

Serious eye damage/eye irritation
Causes serious eye damage.

Components:
Insulin Glargine:
Remarks: No data available
m-Cresol:
Species: Rabbit
Result: Irreversible effects on the eye

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Insulin Glargine:
Remarks: No data available

Germ cell mutagenicity
Not classified based on available information.

Components:

Insulin Glargine:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Remarks: Based on data from similar materials

Test Type: In vitro mammalian cell gene mutation test
Result: negative
Remarks: Based on data from similar materials

Test Type: Chromosome aberration test in vitro
Result: negative
Remarks: Based on data from similar materials

m-Cresol:
Genotoxicity in vitro: Test Type: Chromosome aberration test in vitro
Method: OECD Test Guideline 473
Result: positive

Test Type: Bacterial reverse mutation assay (AMES)
Method: OECD Test Guideline 471
Result: negative

Genotoxicity in vivo: Test Type: Mutagenicity (in vivo mammalian bone-marrow
cytogenetic test, chromosomal analysis)
Species: Mouse
Application Route: Ingestion
Method: OECD Test Guideline 475
Result: negative

Carcinogenicity
Not classified based on available information.
Components:

Insulin Glargine:
- **Species**: Rat
- **Exposure time**: 2 Years
- **NOAEL**: 0.455 mg/kg body weight
- **Result**: negative

Species: Mouse
- **Exposure time**: 2 Years
- **NOAEL**: 0.455 mg/kg body weight
- **Result**: negative

m-Cresol:
- **Species**: Mouse, males
- **Application Route**: Ingestion
- **Exposure time**: 105 weeks
- **Result**: equivocal
- **Remarks**: Based on data from similar materials

Species: Mouse, female
- **Application Route**: Ingestion
- **Exposure time**: 106 - 107 weeks
- **Result**: positive
- **Remarks**: Based on data from similar materials

Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

Reproductive toxicity
Not classified based on available information.

Components:

Insulin Glargine:
- **Effects on fertility**: Test Type: Fertility/early embryonic development
  - **Species**: Rat
  - **Application Route**: Subcutaneous
  - **Fertility**: NOAEL: 0.36 mg/kg body weight
  - **Result**: No effects on fertility

  Test Type: Fertility/early embryonic development
  - **Species**: Rabbit
  - **Application Route**: Subcutaneous
  - **Fertility**: NOAEL: 0.072 mg/kg body weight
  - **Result**: No effects on fertility

- **Effects on foetal development**: Test Type: Embryo-foetal development
  - **Species**: Rat
  - **Application Route**: Subcutaneous
  - **Developmental Toxicity**: NOAEL: 0.36 mg/kg body weight
  - **Result**: No effects on foetal development

Species: Rabbit
Application Route: Subcutaneous
Developmental Toxicity: LOAEL: 0.072 mg/kg body weight
Result: Fetotoxicity
Remarks: The mechanism or mode of action may not be relevant in humans.

m-Cresol:
Effects on fertility: Test Type: Two-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on foetal development: Test Type: Prenatal development toxicity study (teratogenicity)
Species: Rat
Application Route: Ingestion
Result: negative

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (Blood, Nervous system) through prolonged or repeated exposure if swallowed.

Components:
Insulin Glargine:
Exposure routes: Ingestion
Target Organs: Blood, Nervous system
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:
Insulin Glargine:
Species: Rat
NOAEL: 0.5 mg/kg
LOAEL: 1.5 mg/kg
Application Route: Subcutaneous
Exposure time: 30 d
Target Organs: Blood, Nervous system

m-Cresol:
Species: Rat
NOAEL: 150 mg/kg
Application Route: Ingestion
Exposure time: 13 Weeks
Method: OECD Test Guideline 408
Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:
Insulin Glargine:
Inhalation: Target Organs: Blood
Symptoms: Hypoglycemia, Headache, Sweating, Tremors, Nausea

12. ECOLOGICAL INFORMATION

Ecotoxicity
Components:
m-Cresol:
Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): 8.6 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia pulex (Water flea)): > 99.5 mg/l
Exposure time: 48 h

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 1.35 mg/l
Exposure time: 32 d
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia magna (Water flea)): 1 mg/l
Exposure time: 21 d
Remarks: Based on data from similar materials

Persistence and degradability
Components:
m-Cresol:
Biodegradability: Result: Readily biodegradable.
Biodegradation: 90 %
Exposure time: 28 d
Method: OECD Test Guideline 301D

Bioaccumulative potential
Components:
m-Cresol:
Bioaccumulation: Species: Leuciscus idus (Golden orfe)
Bioconcentration factor (BCF): 17 - 20

Partition coefficient: n-octanol/water: log Pow: 1.96
SAFETY DATA SHEET

Insulin Glargine Formulation

Mobility in soil
No data available

Other adverse effects
No data available

13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues : Dispose of in accordance with local regulations.
Contaminated packaging : Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Minister of Industry Regulation No. 23/M-IND/PER/4/2013 concerning the Revision of Minister of Industry Regulation No. 87/M-IND/PER/9/2009 concerning Globally Harmonized System of Classification and Labelling of Chemicals.

Regulation of the Minister of Health No. 472 of 1996 on the Safeguarding of Substances Hazardous to Health
Hazardous substances that must be registered : Not applicable

Government Regulation No. 74 of 2001 on the Management of Hazardous and Toxic Substances
Hazardous substances approved for use : Not applicable
Prohibited substances : Not applicable
Restricted substances : Not applicable
SAFETY DATA SHEET

Insulin Glargine Formulation

Regulation of the Minister of Trade No. 44 of 2009 on Procurement, Distribution and Supervision of Hazardous Materials
Type of Hazardous Materials Restricted to Import, Distribution and Supervision : Not applicable

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

16. OTHER INFORMATION

Further information

Date format : yyyy/mm/dd

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ID OEL : Indonesia. Occupational Exposure Limits
ACGIH / TWA : 8-hour, time-weighted average
ID OEL / NAB : Long term exposure limit

AIIIC - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardisation; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evalu-
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.